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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,222	01/15/2002	Ping Gao	C-3407/1/US	5749

26648 7590 03/03/2005

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,222	GAO ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Request for Continued Examination and Amendment dated 11/23/04.

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 2, 4,5,8 – 16, 20 – 27, 31 – 37, 43 – 45, 48 – 50, 54 – 57, 60, 61, 65 – 70, 72-75 and 84 – 91 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 – 12, 18 – 20, 24 – 32 of copending Application No. 10/119,118. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to an orally deliverable pharmaceutical composition comprising a cyclooxygenase-2-inhibitor, a solvent liquid, turbidity-decreasing polymer, a vasomodulator and/or an alkylxanthine compound. The turbidity-decreasing polymers are identical to those of the instant application. The cyclooxygenase-2-inhibitor, liquid solvents and other active ingredients are identical to those of the instant application. The difference in the set of claims is that the claims of the co-pending application further comprise a free-radical scavenging antioxidant, yet the claims of the

instant application comprise open claim language, which allows for the inclusion of the free-radical scavenging antioxidants. One of ordinary skill in the art would be motivated to interchange the invention of the co-pending application with those of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5,8-12, 14-16, 24-29, 31-40, 43-47, 49,50,58-63, 65-70,72-78, and 82-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*). The claims are drawn to an orally deliverable

pharmaceutical composition comprising a selective cyclooxygenase-2 inhibitor drug, a solvent liquid selected from the group consisting of glycols and glycol ethers and turbidity-decreasing polymers.

Tanida teaches an oral capsule formulation comprising a cellulosic base specifically hydroxypropylmethylcellulose (abstract). The formulation can be in the form of powders or liquids, which are ultimately encapsulated into gelatin capsules (col. 2, lin. 58-65). Many drugs can be included in the formulation, and most preferred are cyclooxygenase-2 inhibitors drugs such as celecoxib (col. 3, lin. 41; lin. 56). When the formulation is a liquid, polyethylene glycol 400 is used as a solvent for the drug, where the drug is completely dissolved in the glycol (col. 4, lin. 14-33).

The reference however lacks an explicit example of the COX-2 inhibitors drugs in combination with glycols and cellulosic polymers; however, the reference suggests that COX-2 inhibitor drugs are the preferred active agents. The reference further suggests the inclusion of polyethylene glycol 400 in a liquid formulation where the active agent (preferred active agent) is completely dissolved and encapsulated in a hydroxypropylmethylcellulose-based capsule. The suggestion is made for the combination whether exemplified in the examples or not, it is the position of the examiner that sufficient guidance is provided to produce an oral COX-2 inhibiting formulation.

Regarding claims reciting specific ranges and concentrations, it is the position of the examiner that such limitations do not impart patentability on the claims since they can be determined through routine experimentation by one of ordinary skill in the art. Tanida provides the suggestions for a liquid oral capsule comprising a COX-2 inhibiting drug, dissolved in a

glycol in a cellulosic-based environment. These disclosures meet the general conditions of the claims. Applicant is reminded that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With these things in mind one of ordinary skill in the art would have been motivated to follow the suggestions and teachings of Tanida in order to provide a stable formulation with improved release profiles, allowing for more manageable treatments. It would have been obvious to skilled artisan to follow these teachings and suggestion with an expected result of an oral liquid filled capsule with improved stability and delivery.

3. Claims 17 – 19, 51 – 53, and 79 – 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*) in view of Hanna et al (USPN 4,601,894). The claims are drawn to a celecoxib composition is recited the COX-2 inhibitor, polyvinylpyrrolidone and cellulosic polymers are recited as possible turbidity-decreasing polymers, and polyethylene glycol is listed as the solvent. For the cellulosic polymer

hydroxypropylmethylcellulose is the preferred excipient. The polymer has about 15% to about 35% methoxyl substitutions and about 3% to about 15% hydroxypropoxyl substitution.

As discussed above Tanida discloses a celecoxib formulation comprising hydroxypropylmethylcellulose. What is lacking in the reference is a disclosure of the particular methoxyl and hydroxypropoxyl substitution concentrations. Hanna et al discloses a formulation comprising a hydroxypropylmethylcellulose with about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropoxyl substitution (col. 2, lin. 43 – 61). The formulation comprises the analgesics acetaminophen and can be formulated into capsules (col. 1, lin. 60 – 63). It would have been obvious to one of ordinary skill in the art to combine the hydroxypropylmethylcellulose of Hanna with the formulation of Tanida since both formulations disclose the delivery of pain relieving medicaments.

With these things in mind a skilled artisan would have been motivated to combine the HPMC of Hanna into the formulation of Tanida in order to provide a stable environment to deliver the liquid COX-2 inhibitor formulation of Tanida. A skilled artisan would have been motivated to modify the concentrations disclosed by Tanida in order to optimize the release and delivery of the celecoxib formulation. It would have been obvious to a skilled artisan at the time of the invention to combine and modify the teachings of the art with an expected result of a stable capsule formulation of celecoxib useful in treating various disorders.

4. Claims 13 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending*

translation of the Japanese document) in view of Guess et al (USPN 6,054,455). The claims are drawn tot a composition where the active agent is valdecoxib.

As discussed above Tanida, disclose celecoxib formulations. Valdecoxib is a well-known COX-2 inhibitor, which can be used in place of or in conjunction with celecoxib. This is seen in Guess, which discloses capsule formulations possibly comprising celecoxib, valdecoxib and other COX-2 inhibitors, in capsule form (col. 32, lin. 27 – 29; col. 33, lin. 18 – 21). Since the compounds are so well known and studied it would be well within the level of skill in the art to substitute the valdecoxib of Guess into the formulation of either Tanida in order to treat pain, especially since COX-2 inhibiting drugs are preferred agents for Tanida.

With this in mind a skilled artisan would have been motivated to substitute the valdecoxib of Guess into the formulations of either Tanida in order to treat a wider variety of disorders and ailments. It would have been obvious to a skilled artisan at the time of the invention to make the substitution with an expected result of a COX-2 capsule formulation capable of treating a variety of disorders.

Claims 20-23, 54-57, and 84-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*) and Black et al (USPN 5,733,909). The claims are drawn to an oral formulation comprising a COX-2 inhibitor of low water solubility, a solvent liquid and a turbidity-decreasing polymer. The composition further comprises an alkylxanthine compound such as caffeine.

As discussed above Tanida discloses a liquid formulation comprising a COX-2 inhibitor, specifically celecoxib dissolved in a glycol. The reference however is silent to the inclusion of an alkylxanthine compound. However the inclusion of such a compound is well within the level of skill in the art as seen in Black, which discloses COX-2 inhibitors in combination with caffeine.

Black et al discloses a capsule formulation comprising COX-2 inhibitors or pharmaceutical salts thereof combined with other active agents such as caffeine and theobromine (col. 7, lin. 52 – col. 8, lin. 60). The formulation comprises liquid PEG, along with hydroxypropylmethylcellulose (col. 10, lin. 30 – 43). Syrup and elixir formulations are also disclosed (col. 11, lin. 19 – 25). A method of treating a patient in need is also disclosed by the reference (col. 11, lin. 7 – col. 12, lin. 38). A skilled artisan would have been able to include the caffeine and theobromine of Black into the formulations of Tanida since both disclose liquid formulations of COX-2 inhibitors.

One of ordinary skill in the art would have been motivated to include the alkylxanthine compounds of Black in to the formulation of Tanida in order to treat a wider array of conditions. It would have been obvious to combine the teachings since both references disclose liquid formulations of COX-2 inhibitors and methods of treating disorders with such formulations. It would have been obvious to combine the teachings and suggestions with an expected result of a liquid formulation able to treat varying disorders more effectively.

5. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation*

of the Japanese document) in view of Kawata et al (USPN 4,343,789). The claim is drawn to a composition comprising a drug of low water solubility in a high-energy state, in capsule form where the capsule wall comprises a cellulosic polymer.

As discussed above Tanida discloses a capsule formulation where the active agent is in a high-energy state (salt thereof), where the wall of the capsule comprises a cellulosic polymer. What is lacking in the reference is a disclosure of the active agents in an amorphous form. The drugs are present in their salt forms however. Kawata discloses amorphous forms of indomethacin (abstract; col. 2, lin. 39 – 44). Tanida discloses a high-energy state of indomethacin as well. It would have been obvious to include the amorphous form of Kawata into the capsule formulation of Tanida since both formulation provide high energy forms of poorly water soluble drugs, Tanida in salt form, and Kawata in amorphous form. A skilled artisan would have followed the suggestion of Kawata in order to improve the solubility of the formulation.

One of ordinary skill in the art would have been motivated to combine the high-energy amorphous form of indomethacin into the capsule formulation of Tanida in order to improve the solubility of the drug and provide a faster release to the active agent. It would have been obvious to skilled artisan to combine the teachings as such, with an expected result of a capsule formulation capable of treating various disorders quickly.

Response to Arguments

1. Applicant's arguments with respect to claims 1-5,8-29,31-40,43-63,65-70,72-91 have been considered but are moot in view of the new ground(s) of rejection. However regarding applicant arguments:

a. Tanida does not provide the selective cyclooxgenase-2 inhibitor drug or the solvent system of applicant.

b. The is no motivation to combine Tanida with any other references (Guess, Black, or Kawata)

2. It is the position of the examiner that Tanida does in fact suggest the invention of the instant claims. Applicant states that celecoxib is a representative example of a COX-2 inhibitory drug that contains the structure claimed. Tanida discloses an oral formulation comprising celecoxib, as do all of the dependent references. Tanida further teaches a liquid formulation that is encapsulated into a hydroxypropylmethylcellulose capsule where the drugs are dissolved in a solvent such as polyethylene glycol 400. These teachings establish the level of skill in the art. Applicant is invited to provide a patentable distinction between the formulations taught by Tanida, until such time the claims will remain obviated.

3. Regarding argument b., the supporting reference merely flush out details such as the specific type of embodiments and additives are known in the art. The references provide combinations that, under the suggestion of Tanida, would be obvious to a skilled artisan. The combinations taught provide a product that meets the limitations of the instant claims. However, The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte*

Gray, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). With these things in mind, the claims will remain obviated.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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